PAGE, SECTION, PARAGRAPH	OLD TEXT	NEW TEXT	REASON FOR CHANGE
Cover page, footers, Global change	Version 1.1, 6/30/2006	Version 1.2, 10/15/2006	Updated protocol version number (1.2) and date (10/15/2007) to reflect current version number and date.
Cover page, footers, Global change	Version 1.2, 10/15/2006	Version 1.3, 11/02/2007	Updated protocol version number to reflect current version number and date.
Page 4, Protocol Summary, Design, 1st paragraph	The trial is designed to show non-inferiority of the non-SOS-PCI arm to the SOS-PCI arm, assuming an expected 30-day adverse event rate of 4.0%, and a 12 month adverse event rate of 10%, for the base case SOS-PCI arm.	The trial is designed to show non-inferiority of the non-SOS-PCI arm to the SOS-PCI arm, assuming an expected 30-day **major** adverse **cardiac** event rate of 4.0%, and a 12 month major adverse **cardiac** event rate of 10%, for the base case SOS-PCI arm.	Added clarification to endpoints.
Page 4, Protocol Summary, Design, 2nd paragraph	The subset will include the first 10% of subjects **consecutively enrolled** at all study sites enrolling subjects in both randomized and nested portions of the trial.	The subset will include a **random sample** of 10% of **subjects selected** from all study sites enrolling subjects in both randomized and nested portions of the trial	Changed language to reflect subjects participating in the angiographic subset.
Page 4, Protocol Summary, Primary Endpoint, 1st paragraph and globally through protocol	The primary safety endpoint is 30-day major adverse cardiac event (MACE) rate, defined as a composite endpoint of the occurrence of either all cause mortality,		Deleted “target vessel” from myocardial infarction. Target vessel and non-target vessel MI will be included in the MACE endpoint.

	target vessel myocardial infarction (Q wave and non-Q wave), repeat coronary revascularization (of the target vessel or non-target vessel) by either percutaneous or coronary artery bypass graft [CABG] methods, or stroke, at 30-days.		
Page 5, Protocol Summary, Secondary Endpoints, and Page 10, Section 2.2.1 Secondary Endpoints		Added: **4. Rate of stent thrombosis at 12 months**	Added additional safety secondary endpoint
Page 5, Protocol Summary, Secondary Endpoints, and Page 10, Section 2.2.1 Secondary Endpoints	5. Rate of urgent revascularization through day 30.	6. Rate of **emergency or** urgent revascularization through day 30.	Added "emergency" since emergency revascularizations are being captured as part of the secondary endpoints.
Page 5, Protocol Summary, Principal Investigator	Study Principal Investigator: Alice K. Jacobs, M.D.	Study Principal Investigator: Alice K. Jacobs, M.D. **Boston University School of Medicine**	Added affiliated institution to Principal Investigator's name

		Boston Medical Center	
Page 6, Protocol Summary, Co-Principal Investigator	Co-Principal Investigators: Sharon-Lise Normand Ph.D. Laura Mauri M.D., M.Sc.	Co-Principal Investigators: Sharon-Lise Normand Ph.D. Laura Mauri M.D., M.Sc. **Harvard Medical School**	Added affiliated institution to Co-Principal Investigators' names.
Page 6, Protocol Summary	Data Coordinating Centers: Harvard Clinical Research Institute Laura Mauri, MD, M.Sc. 930 Commonwealth Avenue Boston, MA 02127 617-632-1515	Data Coordinating Centers: Harvard Clinical Research Institute **Donald Cutlip, MD** Laura Mauri, MD, M.Sc. 930 Commonwealth Avenue Boston, MA 02127 617-632-1515	Added contact name for DCC.
Page 6, Protocol Summary	**Data Coordinating Centers:** MASS-DAC Data Coordinating Center Harvard Medical School Sharon-Lise Normand PhD 180 Longwood Avenue Boston, MA 02215 617-432-3260	**Statistical Analysis Center:** MASS-DAC Data Coordinating Center Harvard Medical School Sharon-Lise Normand PhD 180 Longwood Avenue Boston, MA 02215 617-432-3260	Moved MASS-DAC DCC contact information under new heading.
Page 10, Section 2.1.1, Primary Endpoint	The primary endpoint is defined a composite endpoint of the occurrence of death (from all cause),	The primary endpoint is defined **as major adverse cardiac events (MACE),** a composite endpoint of the occurrence of death (from all cause), myocardial infarction, repeat	Added clarification to primary endpoint

	target vessel myocardial infarction, repeat coronary revascularization, or stroke.	coronary revascularization **(by surgical or percutaneous methods),** or stroke.	
Page 11, Section 3.0, Study Design, 1st paragraph	Assuming an expected 30-day major adverse cardiac event rate of 4.0%, and a 12 month major adverse cardiac event rate of 10%, for the base case SOS-PCI arm, the trial will have a 2.5% one-sided type I error and 90% power to detect a 2.0% difference in 30-day rates, and 3.0% difference in 12 month rates**, differences**.		Edited section by deleting "differences."
Page 11, Section 3.0, Study Design, 2nd paragraph	Specifically, 6000 subjects will be enrolled in a multi-center nested RCT, in which 4800 eligible subjects will be consented and randomized in a 3:1 ratio at the non-SOS hospitals for PCI to be performed at either the enrolling non-SOS hospital (3 chances out of 4) or a corresponding SOS hospital (1 chance out of 4).	Specifically, 6000 subjects will be enrolled in a multi-center, nested, **randomized, controlled trial (RCT)**, in which 4800 eligible subjects will be consented and randomized in a 3:1 ratio at the non-SOS hospitals for PCI to be performed at either the enrolling non-SOS hospital (3 chances out of 4) or a corresponding SOS hospital (1 chance out of 4).	Wrote out acronym for clarification.
Page 11, Section 3.0, Study Design, 3rd paragraph		Added: **Eligible subjects will be recruited from the patient pool of all subjects undergoing**	Added text to clarify recruitment efforts.

		diagnostic catheterization for treatment of known or suspected coronary artery disease at non-SOS and SOS hospitals (subjects undergoing diagnostic catheterization for <u>planned</u> valve surgery or cardiac transplantation are not included in the pool of recruited subjects recorded on the site screening log).	
Page 11, Section 3.0, Study Design, 3rd paragraph		Added: **In both the randomized and nested cohorts, study subjects may choose to have their post-PCI follow-up care performed at their local medical provider's site. The research staff at the study sites may enroll study subjects who choose local follow-up by collaborating with the local medical provider (and staff) to obtain the necessary 30 day and cumulative 12 month follow-up medical information necessary for data collection and determination of study endpoints. Study site coordinators may also contact subjects directly to ascertain their health care status, in addition to collaborating with the subject's local medical provider.**	Added language to clarify clinical assessment follow-up visits.
Page 12, Section 3.0, Study Design, 4th paragraph		Added: **Since this study will evaluate the rates of complications and late-term**	Introduced language to explain staging procedures and when staging is acceptable in the study.

		revascularization, including the need for emergency surgery, between tertiary (SOS) and community (non-SOS) hospitals, staged-revascularization of study subjects is limited to patients with specific medical criteria justifying a staged procedure. Patients who present with the following criteria prior to their index procedure are eligible for a staged procedure and study enrollment: **1. eGFR < 60 ml/min, and/or** **2. creatinine > 1.5 mg/dl** **Additionally, study subjects who qualify for staged procedures by these criteria are also requested to have their second portion of the staged procedure performed no sooner than 14 days unless clinically necessary and at least within 30 days of first procedure at the site to which they were randomized. In this cohort of subjects treated for a pre-approved staged procedure, the period for 30 day endpoint determination of MACE will begin with the first index procedure and extend to 30 days after the second portion of the staged procedure. Similarly, the period for 12 month endpoint determination of MACE begins with the first index procedure and extends to 12 months after the second portion of the**	

		staged procedure.	
Page 12, Section 3.0, Study Design, 6th paragraph	The clinical events committee (CEC) will be blinded to the assigned treatment (PCI setting) arm for the entire study.	The clinical events committee (CEC) will be blinded to the assigned treatment (PCI setting **of SOS vs non-SOS site**) arm for the entire study.	Added language to clarify assigned treatment.
Page 12, Section 3.0 Study Design, 6th paragraph	The subset will include **the first** 10% of subjects **consecutively enrolled** at all study sites enrolling subjects in both randomized and nested portions of the trial.	The subset will include a **random sample of** 10% of **subjects selected from** all study sites enrolling subjects in both randomized and nested portions of the trial.	Changed selection of subjects participating in the angiographic subset for a more objective analysis.
Page 12, Section 3.0 Study Design, last (9th) paragraph	For subjects requiring urgent surgical intervention due to non-SOS PCI procedural complication, the non-SOS hospital must transport the study subject to the SOS partnering hospital providing cardiac surgical support.	For subjects requiring urgent **or emergency** surgical intervention due to non-SOS PCI procedural complication, the non-SOS hospital must transport the study subject to the SOS partnering hospital providing cardiac surgical support.	Emergency interventions are being included in the secondary endpoint.
Page 13, Section 3.1.1 Inclusion Criteria #2	Subject requires single- or multi-vessel percutaneous coronary intervention (PCI) of *de novo* target lesion(s).	Subject requires single- or multi-vessel percutaneous coronary intervention (PCI) of *de novo* **or restenotic** target lesion **(including in-stent restenotic lesions**), **OR** **Subject requires staged procedure based upon pre-catheterization procedure**	Clarified eligibility criteria for target lesion.

		qualifying clinical laboratory values of: • **eGFR < 60 ml/min, and/or** • **creatinine > 1.5 mg/dl**	
Page 13, Section 3.1.1 Inclusion Criteria #3	Subject's lesion(s) is (are) amenable to stent treatment with currently available FDA-approved bare metal **and** drug eluting stents.	Subject's lesion(s) is (are) amenable to stent treatment with currently available FDA-approved bare metal **or** drug eluting stents.	Changed "and" into "or" for better clarification.
Page 13, Section 3.1.1 Inclusion Criteria #4	Subject is an acceptable candidate for CABG.	Subject is an acceptable candidate for **elective, urgent or emergency** CABG.	Elaborated on acceptable eligibility criteria.
Page 13, Section 3.1.1 Inclusion Criteria, #6	*Note: Subjects with non-ST segment elevation myocardial infarction may be enrolled if 2 or more CK-MB blood results show a decrease in CK-MB below the site's upper limit of normal or to below half of its peak level.	*Note: Subjects with non-ST segment elevation myocardial infarction may be enrolled if 2 or more CK-MB blood results show a decrease in CK-MB below the site's upper limit of normal or to below half of its peak level; **however, patients with clinical evidence of acute infarction in progress**	Added additional note regarding the participation of NSTEMI patients to avoid adjudication problems in patients without baseline enzyme or marker elevation.

		should not be enrolled.	
Page 14, Section 3.1.1 Inclusion Criteria, #10	10. Subject has normal coronary arteries or insignificant CAD.	--	Previously added IC deleted.
Page 14, Section 3.1.1 Inclusion Criteria, #11	11. Patients with STEMI > 72 hours ago undergoing PCI of an infarct or non-infarct related artery. For both PCI of the infarct or non-infarct-related artery, protocol inclusion criteria must be fulfilled.	--	Previously added IC deleted.
Page 14, Section 3.1.1 *Angiographic* Inclusion Criteria, #12	12. The target lesion(s) is (are) *de novo* native coronary artery lesion(s) with ≥50 and <100% stenosis (visual estimate), or the target lesion is an	10. The target lesion(s) is (are) *de novo* or restenotic (including in-stent restenotic) native coronary artery lesion(s) with ≥50 and <100% stenosis (visual estimate), or the target lesion is an acute (less than 1 month) total occlusion as evidenced by clinical symptoms.	"or restenotic…" added to de novo to match general Inclusion Criterion # 2. List Number also changes b/c of previous deletions.

	acute (less than 1 month) total occlusion as evidenced by clinical symptoms.		
Page 14, Section 3.1.2 Exclusion Criteria, #2	Evidence of ST segment elevation myocardial infarction within **48** hours of the intended treatment.	2. Evidence of ST segment elevation myocardial infarction within **72** hours of the intended treatment **on infarct related or non-infarct related artery**, **or other signs and symptoms of an infarction in development as evidenced by clinical symptoms or cardiac enzyme results (except as permitted in inclusion criterion #6 above). <u>Note</u>: Subjects undergoing PCI of a non-infarct related artery within 72 hours of STEMI are excluded.**	Added language to clarify that patients with evidence of ongoing infarction including clinical EKG evidence or typical rising biomarker levels (as defined by the ACC) up to 72 hours prior to randomization should not be enrolled in the trial.
Page 15, Section 3.1.2 Exclusion Criteria #10		Added: **Note: This exclusion criterion does not apply to post-STEMI patients.**	Added for clarification

Page 15, Section 3.1.2 Angiographic Exclusion Criteria #16		Added: **Subject has normal coronaries or insignificant (i.e. coronary lesion(s) < 50% stenosis).**	Since many subjects were being excluded for their "normal coronaries" and coordinators were referencing inclusion criteria #2 (i.e. subject requires single- or multivessel-PCI of de novo or restenotic target lesion) to explain subject's non-enrollment, an appropriate exclusion criterion was added to reflect this oft cited characteristic.
Page 15, Section 3.1.2 Angiographic Exclusion Criteria #17	The target vessel is associated with ST-segment elevation MI.	The target vessel is associated with **(an acute)** ST-segment elevation MI.	Added language to clarify STEMI exclusion.
Page 15, Section 3.1.2 Angiographic Exclusion Criteria			Numbering of angiographic exclusion criteria has changed to reflect new additions.
Page 15, Section 3.1.2 Angiographic Exclusion Criteria #18	Any target vessel has evidence of excessive thrombus (e.g. requires target vessel thrombectomy) or tortuousity (>60 degree angle) that makes it unsuitable for proper	Any target vessel has evidence of: a. excessive thrombus (e.g. requires target vessel thrombectomy) b. tortuousity (>60 degree angle) that makes it unsuitable for proper stent delivery and deployment,	Reformatted criteria for better readability. Treatment of heavy calcification was excluded as it is not appropriate for this trial of standard PTCA and stenting.

	stent delivery and deployment.	**c. heavy calcification.**	
Page 15, Section 3.1.2 Angiographic Exclusion Criteria #20	Any lesion is located in a saphenous vein graft.	Any lesion is located in a saphenous vein graft, **however, lesions located within the native vessel but accessed through the graft are eligible.**	Added language to clarify eligible and ineligible lesions in the SVG.
Page 15, Section 3.1.2 Angiographic Exclusion Criteria #20	Any lesion is located in a saphenous vein graft, however, lesions located within the native vessel but accessed through the graft are eligible	Any lesion that is located in a saphenous vein graft, however, lesions located within the native vessel but accessed through the graft are eligible	Wording clarification
Page 16, Section 3.2	3.2 Informed Consent **and Subject Recruitment**	3.2 Informed Consent **3.3 Subject Recruitment**	Deleted "and subject recruitment" from header and created a new section entitled "Subject Recruitment"
Page 16, Section 3.2 Informed Consent		**Eligible subjects will be recruited and consented from the patient pool of all subjects undergoing diagnostic catheterization for treatment of known or suspected coronary artery disease at non-SOS and SOS hospitals (subjects undergoing diagnostic catheterization for <u>planned</u> valve surgery or cardiac**	Due to inappropriate subjects in the screening logs, added a better explanation for which subjects should be recruited and those who should not be approached (e.g. patients undergoing valve surgery).

		transplantation are not included in the pool of consented and recruited subjects recorded on the site screening log).	
Page 16 Section 3.2 Informed Consent, 1st paragraph	Eligible subjects will be recruited and consented from the patient pool of all subjects undergoing diagnostic catheterization for treatment of suspected coronary artery disease at non-…	Eligible subjects will be recruited and consented from the patient pool of all subjects undergoing diagnostic catheterization for treatment of known or suspected coronary artery disease at non-…	Reworded for clarity
Page 16 Section 3.2 Informed Consent, 2nd and 3rd paragraphs	Subjects recruited for randomization at non-SOS hospitals will sign a consent form… Subjects participating in the nested control group at a SOS hospital will sign a separate informed consent document…	***Randomized Subjects:*** Subjects recruited for randomization at non-SOS hospitals will sign a consent form… ***Nested Subjects:*** Subjects participating in the nested control group at a SOS hospital will sign a separate informed consent document…	Added "randomized subjects" and "nested subjects" headers for better readability.
Page 16, Section 3.2 Informed Consent, 2nd paragraph		Added: **Depending upon institutional requirements, subjects may be asked to sign an additional informed consent form at the SOS site after randomization.**	Due to study site inquiries, clarified the informed consent forms that may be required.

Page 16, Section 3.2 Informed Consent, 3rd paragraph		Added: **SOS sites will be informed of their recruitment dates, which will be randomly selected for them by the Data Coordinating Center. Recruitment should only be performed on the assigned recruitment dates.**	Clarified SOS recruitment procedures for nested subjects.
Page 16, Section 3.3 Subject Recruitment (new section)	Subject screening and eligibility will be documented on the *Subject Screening and Eligibility Log* for all subjects who sign informed consent. Research personnel at each site will record the criteria by which subjects are excluded or will record the date of subject enrollment. Adult patients will be enrolled without regard to age or sex and will be included or excluded from enrollment based upon the inclusion and exclusion criteria listed above.	Subject screening and eligibility will be documented on the *Subject Screening and Eligibility Log* for all subjects who sign informed consent. **The purpose of the screening log is to capture all patients screened for consideration of enrollment into the study and includes collection of : screening date, screening number, name code initials, gender, age, whether the consent form was signed, consent date (if applicable), eligibility (both clinical and angiographic), randomization, whether a stage procedure is needed or planned, and additional comments.** Research personnel at each site will record the criteria by which subjects are excluded or will record the date of subject enrollment. Adult patients will be enrolled without regard to age or sex and will be included or excluded from enrollment based upon the inclusion and exclusion criteria listed above. **Completed screening logs should be submitted to the Data Coordinating Center (HCRI) on a weekly**	Added language to clarify screening log purpose and instruction.

		basis.	
Page 16, Section 3.3 Subject Recruitment	Subject screening and eligibility will be documented on the *Subject Screening and Eligibility Log* for all subjects who sign informed consent….	Subject screening and eligibility will be documented on the *Subject Screening and Eligibility Log* for all subjects.…	Reworded to include all subjects
Page 17, Section 3.4 Randomization, first and second paragraphs	Randomization will occur through the use of a sealed envelopes located in the cardiac catheterization laboratory (excluding subjects enrolled in the nested study cohort). The randomization of subjects will be stratified based upon diabetic status (presence or absence).	Randomization will occur through the use of sealed envelopes located in the **enrolling** non-SOS cardiac catheterization laboratory (excluding subjects enrolled in the nested study cohort). The randomization of subjects will be stratified based upon diabetic status (presence or absence). **The patient is considered enrolled into the study when the patient is randomized.** **Responsibility for communicating SOS site availability for accepting transfer is critical for allowing randomization and recruiting of patients. SOS hospitals must inform their enrolling non-SOS partner hospital if the SOS hospital is diverting patients; procedures should not be performed at non-SOS hospital until the SOS hospital is back "on-line". In addition, the intent is for most patients to be treated on the same days as the randomization is performed. If beds at an SOS hospital are not immediately available, the partnering non-SOS hospital should not randomize**	Added language to clarify randomization assignment and responsibilities.

		patients to that SOS hospital.	
Page 17, Section 4.2 Determination for Study-Permitted Staged Procedures		Added: **4.2 DETERMINATION FOR STUDY-PERMITTED STAGED PROCEDURES** **Staged-revascularization of study subjects is limited to patients with specific medical criteria justifying a staged procedure. Patients who present with the following criteria prior to their index procedure are eligible for a staged procedure and study enrollment based upon laboratory values documented prior to randomization:** **1. eGFR < 60 ml/min, and/or** **2. creatinine > 1.5 mg/dl** **For all other patients, including those in whom it is uncertain whether a second stenosis will require revascularization, planned staging is not recognized and therefore a repeat procedure will be considered an endpoint.** **In this study, it is required that staged procedures be performed for only the criteria stated above, and clinical monitoring will be performed to ensure evidence of these criteria existed prior to randomization. Investigators must**	Added section 4.2 to include language regarding when staging procedures are allowed in the study.

		document on the case report forms this planned staging and laboratory values supporting the interventionalist's decision to stage the procedure.	
Page 18 – 24, Sections 4.3 Baseline Procedures through Section 4.11 Study Termination			The numbering of Section 4.0 sub-headings has changed to reflect the new addition of Section 4.2 Determination for Study-Permitted Staged Procedures.
Page 18, Section 4.3 Baseline Procedures, 5th bullet	• Assessment of left ventricular function by echocardiography or left ventriculography within 30 days of the procedure.	• Assessment of left ventricular function **by any invasive or non-invasive method (e.g.,** left ventriculography or echocardiography) within 30 days of the procedure **(pre-randomization).**	Created more general language for assessing left ventricular function as to not mandate a particular method. 10/11/07 word order switched.
Page 19, Section 4.4 Concomitant Medications, Table2 , procedure column	Per routine hospital practice At least 325 mg QD 300-600 mg loading dose	**Administer** per routine hospital practice **for purpose of elective PCI procedure** At least 325 mg QD **or per routine hospital practice for purpose of elective PCI procedure** **Administer** 300-600 mg loading dose	Added language for concomitant medication clarification and allowed flexibility for hospital standard institutional practices.
Page 19, Section 4.4 Concomitant Medications, Table 2 , Timing	Post-**Procedure**	Post-**Implant**	Changed "procedure" to "implant" to clarify that concomitant medication time points reflect immediately after implantation of stent.

column			
Page 20, Section 4.5.1 Stent Implant Procedure, 4th paragraph	Limit post dilatation to within the boundaries of the stent.	Limit post dilatation to within the boundaries of the stent. **The use of IVUS may be performed at the discretion of the interventionalist.**	Added language to allow IVUS use.
Page 20, Section 4.5.3 Non-Intervention Post Randomization (new section)		**4.4.3 Non-Intervention Post Randomization** **If the randomized subject does not undergo PCI with implantation of a stent, the reason for non-intervention must be documented in the eCRF by the interventionalist making the decision to not perform PCI post randomization.**	Added instructions for situations in which subject randomized doesn't undergo PCI.
Page 20, Section 4.6 Post Procedure	• Heparin or bivalirudin should be continued or discontinued, per hospital standard • ACT should be monitored per hospital standards • Vascular sheaths should be removed per hospital standards	• Heparin or bivalirudin should be continued or discontinued, per hospital standard **practice** • ACT should be monitored per hospital standard **practice** • Vascular sheaths should be removed per hospital standard **practice**	Added language for clarity.
Page 21, Section 4.8.1 Thirty-day	Study subject follow-up clinic evaluation must occur	Study subject follow-up clinic evaluation must occur at 30-days (+ 7 days) post-	Add language to qualify acceptable follow-up time points for staged

Follow-up (Clinic), 1st paragraph	at 30-days (+ 7 days) post-procedure.	procedure. **For subjects with qualifying staged-procedures, this 30 day follow-up assessment occurs 30 days (+7 days) post the second staged procedure and data will be recorded for events that occur between the first index procedure and 30 days after the second staged procedure.**	procedure.
Page 21, Section 4.8.1 Thirty-day Follow-up (Clinic), 2nd bullet	• Study endpoint events of death, MI, stroke and bleeding complications,	• Major study endpoint events of death, MI, stroke and **major vascular complications and** bleeding complications,	Added clarification to endpoint definition.
Page 21, Section 4.8.1 Thirty-day Follow-up (Clinic), 4th bullet	• Any interventional treatment that occurred since the previous contact (*e.g.*, repeat revascularization). This will include documentation regarding subject need for revascularization based upon clinical status, and	• Any interventional treatment that occurred since the previous contact (*e.g.*, repeat revascularization **by surgical or percutaneous methods**). This will include documentation regarding subject need for revascularization based upon clinical status, and	Clarified definition of repeat revascularization.
Page 22, Section 4.8.2 Twelve Months Post-	A clinic visit will occur at 12 months (±30 days) post-	A clinic visit will occur at 12 months (±30 days) post-procedure. **For subjects with**	Added text to qualify acceptable follow-up time points for staged procedure.

Procedure (Clinic), 1st paragraph	procedure and will consist of:	**qualifying staged-procedures, this 12 months follow-up assessment occurs 12 months (+30 days) post the second staged procedure. Data will be recorded for events that occur between the first index procedure and through 12 month after completion of the second staged procedure. This visit** will consist of:	
Page 22, Section 4.8.2 Twelve Months Post-Procedure (Clinic), 2nd bullet	• Study endpoint events of death, MI, and stroke,	• Major study endpoint events of death, MI, and stroke,	Clarified study endpoint events.
Page 22, Section 4.8.3 Additional Angiography and Revascularization, 1st paragraph	All subsequent angiograms or revascularizations performed on the target vessel during the 12 month follow-up period should be preceded by a physician evaluation during which the physician will indicate whether or not the subject's clinical status warrants revascularization.	All subsequent angiograms or revascularizations performed on the target vessel during the 12 month follow-up period should be preceded by a physician evaluation during which the physician will indicate whether or not the subject's clinical status warrants revascularization. **Any subsequent revascularization procedures should not be performed at non-SOS hospitals with the exception of patients with STEMI as per standard practice at the non-SOS site.**	Added language to ensure that subsequent revascularization is not performed at non-SOS hospitals.
Page 23, Section 4.8.3. Additional Angiography and Revascularization, Table3, Schedule	12 Months (± 30 days) **to End of Study** Follow-Up Visit	12 Months (± 30 days) Follow-Up Visit	Deleted unnecessary words.

of Events, Last Column Heading			
Page 23, Section 4.8.3. Additional Angiography and Revascularization, Table3, Schedule of Events, Row CBC	CBC **with differential and chemistry panel**	CBC	Differential and chemistry panel are not required for this study.
Page 23-24, Section 4.8.3. Additional Angiography and Revascularization, Table3, Schedule of Events, Row Cardiac Enzymes, CK, CK-MB, and Footnote	Cardiac Enzymes, CK, CK-MB	Cardiac Enzymes, CK, CK-MB[2] Added: **[2] If the first two consecutive CK and CK-MB measurements are both normal (e.g. no elevation is observed), the third enzyme measurement is not required. Missing enzyme values due to two consecutive and normal test results, or due to patient's early discharge home prior to the third timeframe blood draw, are not deemed protocol violations. In addition, if institutional procedures prevent testing of CK-MB when CK value is normal, sites must arrange to have CK-MB measured on normal CK values post procedure.**	Added footnote to reflect CK and CKMB requirements and what constitutes a protocol deviation.
Page 24, Section 4.8.3. Additional Angiography and Revascularization, Table3, Schedule of Events, Row Angiography and	X[2]	X[3] Added: **[3] Final eligibility and randomization is based upon angiographic eligibility criteria.**	Changed footnote number to reflect new footnote addition.

Randomization, and Footnote			
Page 24, Section 4.9 Transport for Surgical Intervention, 2nd paragraph		Added: **Each SOS hospital must inform its enrolling non-SOS partner site if the SOS site is diverting patients; randomization or PCI should not be performed at the non-SOS sites until the SOS hospital is back "on-line" and accepting patient transfers.**	Added language to emphasize necessary communication between non-SOS hospitals and their sister sites.
Page 24, Section 4.9 Transport for Surgical Intervention, 3rd paragraph	Data collection in the instance of urgent surgical intervention requires that the time of procedural complication, request for ambulance transport, arrival at surgical hospital and time of surgical intervention be recorded. Every effort must be made to ensure that surgical intervention begins within 120 minutes of procedural complication and interventionalist's decision to transport for emergency surgical intervention.	Data collection in the instance of urgent **and emergency** surgical intervention requires that the time of procedural complication, request for ambulance transport, arrival at surgical hospital and time of surgical intervention be recorded. Every effort must be made to ensure that **the emergency** surgical intervention begins within 120 minutes of procedural complication and interventionalist's decision to transport for emergency surgical intervention.	Added "emergency" language to be consistent.
Page 24, Section 4.10, Repeat Revascularization		Added:	Language added to emphasize that repeat revascularization will only be performed at SOS sites.

Procedures (new section)		**4.9 REPEAT REVASCULARIZATION PROCEDURES** **If subjects require repeat revascularization at any time (beginning from the time the interventionalist completes the index procedure and subject first exits the catheterization lab), the repeat procedure will be conducted at the SOS-partner study site. This requirement does not apply to those subjects who had permitted staged procedures for qualifying for clinical criteria as outlined in section 4.2.** **For those subjects with qualifying staged procedures, any repeat revascularization (beginning from the time the subject exits the catheterization lab after completion of the second portion of the staged procedure) will be conducted at the partner SOS study site with the exception of patients with STEMI as per standard practice at the non-SOS site.**	
Page 29, Section 6.0 Definitions, Bleeding Complications	**BLEEDING COMPLICATIONS** Defined as a procedure related hemorrhagic event that requires a transfusion or surgical repair.	**BLEEDING COMPLICATIONS** Defined as a **study** procedure related hemorrhagic event that **is associated with a fall in hemoglobin of ≥ 3gm/dl or** requires surgical repair.	Added clarification that definition relates to study procedure only.

Page 31, Section 6.0 Definitions, Elective Percutaneous Coronary Intervention (new)		**ELECTIVE PERCUTANEOUS CORONAR INTERVENTION** **Defined as a planned percutaneous coronary intervention performed on a (for our purposes, "elective" means non-emergency) non-emergency basis to treat blockage that is ≥50% and is believed to be the source of ischemic coronary symptoms.**	Added definition to distinguish between elective, urgent and emergency PCI.
Page 31, Section 6.0 Definitions, Emergent Revascularizaton	**EMERGENT REVASCULARIZATION** Defined as **repeat percutaneous coronary intervention or coronary bypass surgery performed on an urgent or emergent basis for severe vessel dissection or closure, or treatment failure resulting in new ischemia.**	**EMERGENCY REVASCULARIZATION** Defined as **immediate transfer for surgery related to a procedural complication or immediate repeat PCI or surgery for stent thrombosis or vessel occlusions that occur after leaving the cath lab.**	Added definition to distinguish between urgent and emergency revascularization. Changed "emergent" to "emergency" globally throughout protocol.
Page 32, Section 6.0 Definitions, Major Adverse Cardiac Event (MACE)	**MAJOR ADVERSE CARDIAC EVENT (MACE)** Defined as a composite endpoint of all cause mortality, **target vessel** myocardial infarction (Q wave and non-Q wave), repeat coronary	**MAJOR ADVERSE CARDIAC EVENT (MACE)** Defined as a composite endpoint of all cause mortality, myocardial infarction (Q wave and non-Q wave), repeat coronary revascularization of target vessel or non-target vessel (PTCA or CABG), or stroke.	Deleted target-vessel from definition since both target-vessel and non-target vessel will be included.

	revascularization of target vessel or non-target vessel (PTCA or CABG), or stroke.		
Page 32, Section 6.0 Definitions, Myocardial Infarction	**MYOCARDIAL INFARCTION** A positive diagnosis of myocardial infarction **of the target vessel** is made when one of the following criteria is met:	**MYOCARDIAL INFARCTION** A positive diagnosis of myocardial infarction is made when one of the following criteria is met:	Deleted "target vessel" because MI can occur in target vessel or non-target vessel.
Page 33-35, Section 6.0 Definitions, Stent Thrombosis	**STENT THROMBOSIS** **Defined as angiographic thrombus or subacute closure within the stented vessel at the time of the clinically driven angiographic re-study for documented ischemia (chest pain and ECG changes). Any death not attributed to a non-cardiac cause within the first 30 days is considered a surrogate for stent thrombosis in the absence of documented angiographic stent patency.**	*Text is large; please see protocol pages 33-35 for added definition.*	Because of post FDA-DES panel meeting, added up-to-date stent thrombosis ARC definition.

Page 35, Section 6.0, Definitions		**TARGET LESION** **The target lesion is the treated segment starting 5 mm proximal to the stent and ending 5 mm distal to the stent.**	Added target lesion definition
Page 35, Section 6.0 Definitions, Target Vessel (new)		**TARGET VESSEL (TV)** **The target vessel is the entire major coronary vessel proximal and distal to the target lesion including upstream and downstream branches and the target lesion itself. (For example: if the original lesion is the first obtuse marginal branch, the target vessel includes the left main coronary artery, the circumflex coronary artery and its branches).** **Note: in three-vessel treatment every repeat revascularization becomes TVR.**	Added target vessel definition for clarification.
Page 36, Section 6.0 Definitions, Urgent Revascularization (new)		**URGENT REVASCULARIZATION** **Surgery or repeat PCI required within 72 hours of index procedure or within 72 hours of acute recurrent ischemic event and related to recurrent or ongoing ischemia or otherwise unsuccessful index procedure.**	Added definition to distinguish revascularization as urgent or emergency.
Page 37, Section 7.1 Clinical Follow-up, 2nd paragraph	In a subset of **consecutive** patients (N=600) angiographic films will be submitted for analysis performed by a blinded core laboratory, to assess baseline	In a **randomly selected** subset of patients (N=600) angiographic films will be submitted for analysis performed by a blinded core laboratory, to assess baseline angiographic characteristics, pre- and post-procedure lesion characteristics, completeness and	Changed selection procedure for angiographic subset to ensure a more objective analysis.

	angiographic characteristics, pre- and post-procedure lesion characteristics, completeness and appropriateness of revascularization.	appropriateness of revascularization.	
Page 38, Section 8.3 Data Collection, 1st paragraph	Research coordinators at each clinical site will perform primary data collection drawn from source document (hospital chart) reviews. Data will be entered by the site personnel into eCRFs on the internet-based EDC system. This will ensure data are forwarded to HCRI in an expedited fashion. HCRI will provide clinical monitoring, including review of EDC data with verification to the source documentation. This will include operator worksheets retained with eCRF documentation and hospital charts.	Research coordinators at each clinical site will perform primary data collection drawn from source document (hospital chart) reviews. Data will be entered by the site personnel into eCRFs on the internet-based EDC system. This will ensure data are forwarded to HCRI in an expedited fashion. **If a subject is randomized to a SOS hospital from the enrolling non-SOS hospital, the research coordinator from the SOS hospital will enter the data from their patients who were treated through discharge. The enrolling non-SOS hospital research coordinators are then ultimately responsible for ensuring that all the patients' follow-up data are entered into the study database through the EDC system.** HCRI will provide clinical monitoring, including review of EDC data with verification to the source documentation. This will include operator worksheets retained with eCRF documentation and hospital charts.	Added language to clarify ownership and responsibility of subject data between non-SOS hospitals and sister sites.
Page 39, Section	Within **7** days hours of	Within **24** hours of knowledge of event	Since study endpoint is MACE,

8.4 Time Windows for Expected Completion of Electronic Case Report Forms/Reports, Table 4, Time of Notification column	knowledge of event		notification must occur within 24 hours, not 7 days.
Page 39, Section 8.4, Table 4, Study Exit form last row.	Within 7 days hours of subject visit	Within 7 days of subject visit	Removed extra word.
Page 40, Section 9.4 Audits/Inspections	In the event that audits are initiated by the sponsors or its **delegate** or local regulatory authority, the investigator shall allow access to the original medical records and provide all requested information.	In the event that audits are initiated by the sponsor's **representative (HCRI)** or local regulatory authority, the investigator shall allow access to the original medical records and provide all requested information.	Clarified that sponsor's representative is HCRI.
Page 41, Section 10.1 Executive Operations Committee, 2nd paragraph		Added: **The Executive Operations Committee may appoint an Independent Review Committee to review cases of protocol violations where PCI was not performed post-randomization. The review will consist of clinical and angiographic evidence in the medical record and reason provided by**	Added language describing Independent Review Committee for Protocol Deviations.

		post-randomization interventionalist who makes the decision to forego PCI in the randomized patient. It is expected that such independent case review will be rarely required throughout the study, but will be performed for each instance when PCI is not performed post-randomization. Subjects randomized but not treated with PCI will remain in the randomized and analyzed subject population. Members of the Independent Review Committee will be announced to all site PIs.	
Page 41, Section 10.1 Executive Operations Committee, table	Alice Jacobs Laura Mauri Sharon-Lise Normand Donald Cutlip Paul Dreyer TBD TBD	Alice Jacobs, **MD** Laura Mauri, **MD, MSc** Sharon-Lise Normand, **PhD** Donald Cutlip, **MD** Paul Dreyer, **PhD** **Joseph Carrozza, MD** **Anthony Marks, MD**	Added professional titles to Executive Operations Committee members and identified the SOS and Non-SOS hospital Representatives.
Page 42, Section 10.2 Clinical Events Committee	The Clinical Events Committee is made up of interventional and non-interventional cardiologists who are not participants in the study. The Clinical Events Committee is charged with the development of specific criteria used for the categorization of clinical	The Clinical Events Committee is made up of interventional and non-interventional cardiologists who are not participants in the study. **The Clinical Events Committee will meet regularly to review and adjudicate all clinical endpoints.** The Clinical Events Committee is charged with **the adjudication of clinical endpoint events according to the definitions outlined in the protocol.** At the onset of the trial, the Clinical Events	Added language to clarify expected responsibilities of the CEC. The CEC will not be adjudicating all clinical events, only clinical endpoints as defined in the protocol.

	events and clinical endpoints in the study. At the onset of the trial, the Clinical Events Committee will establish explicit rules outlining the minimum amount of data required, and the algorithm followed in order to classify a clinical event. All members of the Clinical Events Committee will be blinded to the primary results of the trial. Once the specific criteria for clinical **events and** endpoints are established by the Clinical Events Committee, the Harvard Clinical Research Institute (HCRI) will be responsible for categorizing all clinical events when all necessary data are available. **The Clinical Events Committee will meet regularly to review and adjudicate all clinical events in which the required minimum data is**	Committee will establish explicit rules outlining the minimum amount of data required, and the algorithm followed in order to classify a clinical **endpoint** event. **The Committee will also review and rule on all deaths that occur throughout the trial.** All members of the Clinical Events Committee will be blinded to the primary results of the trial. Once the specific criteria for clinical endpoints are established by the Clinical Events Committee, the Harvard Clinical Research Institute (HCRI) will be responsible for categorizing all clinical **endpoint** events when all necessary data are available.	

	not available. The Committee will also review and rule on all deaths that occur throughout the trial.		